peptide selection

 $\downarrow$ 

peptide optimization

J

formation of Fc-peptide DNA construct

l

insertion of construct into expression vector

↓

transfection of host cell with vector

T

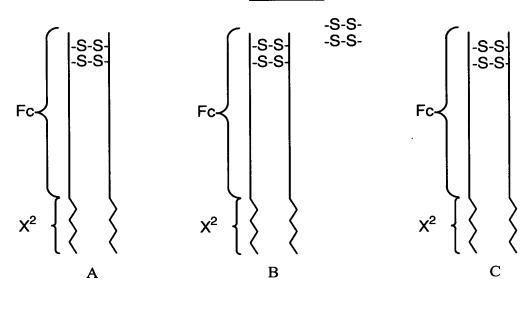
expression of vector in host cell

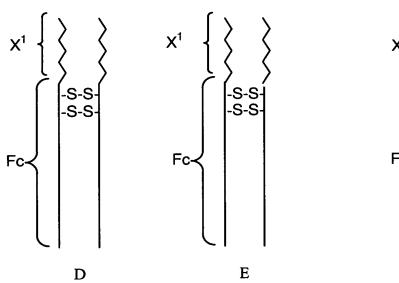
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Fc multimer formation in host cell

J

isolation of Fc multimer from host cell

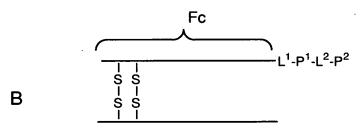


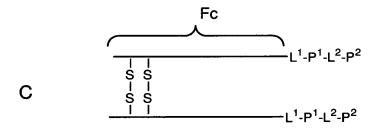


F









	_	ATGGACAAAACTCACATGTCCACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCGTCA	60
	]	1+++++	60
a		M D K T H T C P P C P A P E L L G G P S	-
		GTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTC	100
	61	CAGAAGGAGAAGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAG	120
a		V F L F P P K P K D T L M I S R T P E V	-
		ACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG	100
	121	TGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCAC	180
a		T C V V V D V S H E D P E V K F N W Y V	-
	181	GACGCCTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACG	240
	101	CTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGC	240
a		D G V E V H N A K T K P R E E Q Y N S T	-
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		ATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATG	300
a		Y R V V S V L T V L H Q D W L N G K E Y	-
	301	AAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCC	360
		TTCACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGG	
a		K C K V S N K A L P A P I E K T I S K A	-
	361	AAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACC	420
		TTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGG	
a		K G Q P R E P Q V Y T L P P S R D E L T	•
	421		480
		TTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCAC	
a		K N Q V S L T C L V K G F Y P S D I A V	-
	481	GAGTGGGAGACAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGAC	540
_		E W E S N G O P E N N Y K T T P P V L D	_
a		TCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG	
	541	AGGCTGCCGAGGAAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTC	600
a		S D G S F F L Y S K L T V D K S R W Q Q	-
u		GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAG	
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a		G N V F S C S V M H E A L H N H Y T Q K	-
		AGCCTCTCCCGGGTAAA	
	661	TCGGAGAGGGACAGAGGCCCATTT	
a		S L S L S P G K	

		XDAI	
	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC	60
С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	61	CACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAAC	120
с		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	121	CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA	180
С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	181	GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG	240
С		$\begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	241	CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA	300
С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	301	CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG	360
c		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	361	CCCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC	420
С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	421	AGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT	480
С		TCCACATGTGGGACGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA V Y T L P P S R D E L T K N Q V S L T C	-
	481	GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC	540
С		CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCG L V K G F Y P S D I A V E W E S N G Q P	-
	541	CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT+ GCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGAAGAAGAAGAAGAAGAAGAAGAAGAAG	600
С		E N N Y K T T P P V L D S D G S F F L Y	-
	601	ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG+ TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC	660
С		S K L T V D K S R W Q Q G N V F S C S V	-
	661	TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA + CTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT	720
С		M H E A L H N H Y T Q K S L S L S P G K	-
	721	AAGGTGGAGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGCTTGCT	780
C		G G G G I E G P T L R Q W L A A R A *	-
		BamHI 	

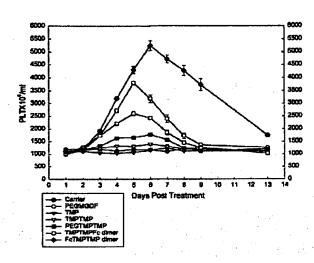
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С	1	AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCTGTTTTGAGTGTGTACAG M D K T H T C P	
	61	CACCTTGTCCAGCTCCGGAACTCCTGGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAAC	120
c		PCPAPELLGGPSVFLFPPKP	-
	121	CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA+ GGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCACCTGCACT	180
С		K D T L M I S R T P E V T C V V D V S  GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG	-
С	181	CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC H E D P E V K F N W Y V D G V E V H N A	
	241	CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA	300
С		GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGT K T K P R E E Q Y N S T Y R V V S V L T	-
С	301	CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG GGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGTTTC V L H Q D W L N G K E Y K C K V S N K A	
c	361	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	421	AGGTGTACACCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT TCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA	480
С		V Y T L P P S R D E L T K N Q V S L T C  GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGCCAGC	-
С	481		540 -
	541	CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT	600
С		E N N Y K T T P P V L D S D G S F F L Y  ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG	-
С	601	TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC S K L T V D K S R W Q Q G N V F S C S V	
c	661	TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGGTA  ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT  M H E A L H N H Y T Q K S L S L S P G K	
С	721	AAGGTGGAGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG	
	781	GTGGTGGAGGTGGCGGAGGTATTGAGGGCCCAACCCTTCGCCAATGGCTTGCAGCAC	
С		CACCACCTCCACCGCCTCCATAACTCCCGGGTTGGGAAGCGGTTACCGAACGTCGTG G G G G G I E G P T L R Q W L A A R	-
		BamHI 	
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	041	CGCGTATTAGAGCTCCTAGGC	

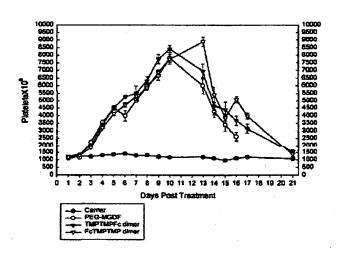
С

	2	ChaI	
	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGATCGAAGGTCCGACTCTGC	60
c	1	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	61	GTCAGTGGCTGGCTGGCGGTGGCGGGGGGGGGGGCATTGAGGGCCCAA+ CAGTCACCGACCGACGACGACGACGACGCCACCACCGCCTAACTCCCGGGTT	120
С		Q W L A A R A G G G G G G G I E G P T  CCCTTCGCCAATGGCTTGCAGCACGCGCAGGGGGAGGCGGTGGGGAAAACTCACACAT	-
c	121	GGGAAGCGTTACCGAACGTCGTGCGCGTCCCCCTCCGCCACCCCTGTTTTGAGTGTGTA L R Q W L A A R A G G G G G D K T H T C	
	181	GTCCACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCCTCTTCCCCCCAA	240
c		CAGGTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGGAGAGGGGGGTTPPPCPAPELLGGPPSVFLFPPK	-
c	241	AACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG  TTGGGTTCCTGTGGGAGTACTAGAGGGCCTTGGGGACTCCCAGTGTACGCACCACCACCACCTGC P K D T L M I S R T P E V T C V V V D V	
	301	TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATA	360
С		ACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTAT S H E D P E V K F N W Y V D G V E V H N	-
С	361	TACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCACCACCAGTCGCACG A K T K P R E E Q Y N S T Y R V V S V L	
с	421	TCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACA  AGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGT  T V L H Q D W L N G K E Y K C K V S N K	
	481	AAGCCCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAAC TTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTT	
С	541	A L P A P I E K T I S K A K G Q P R E P  CACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGA	
С	241	GTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACT Q V Y T L P P S R D E L T K N Q V S L T	
c	601	CCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGC  GGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCG  C L V K G F Y P S D I A V E W E S N G Q	660 -
С	661	AGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCC  TCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGG PENNNYKTPPPVLDSDGSSFFL	720 -
c	721	TCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCT +	780
	781	CCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG	840
С	841	V M H E A L H N H Y T Q K S L S L S P G  BamHI  GTAAATAATGGATCC  855	

С

	2	KbaI	
с	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAGATAACATATGATCGAAGGTCCGACTCTGC  AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACTAGCTTCCAGGCTGAGACG  M I E G P T L R	
c	61	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	121	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	181	AGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACCTCAGCC  TCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCACCTGCACTCGG D T L M I S R T P E V T C V V V D V S H	
С	241	ACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCA  **TGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTACGGT  E D P E V K F N W Y V D G V E V H N A K	
c	301	AGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCG TCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTCGTGCACCACCAGCCAG	
c	361	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	421	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<b>4</b> 80 -
c	481	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	541	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	601	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	661	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	721	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	781	BamHI   AATGGATCC789 TTACCTAGG	





С

	3	KbaI	
	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC	60
С	_	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	61	CACCTTGTCCAGCTCCGGAACTCCTGGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAAC	120
С		P C P A P E L L G G P S V F L F P P K P	-
	121	CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA	180
c	61 121 181 241 301 421 481 541 601	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	191	GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATG	240
С	101	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	-
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С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	301	CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG	360
С		$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
		CTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC	420
С	301	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	421	AGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT	480
С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	481		540
С		CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCG L V K G F Y P S D I A V E W E S N G Q P	-
	541	CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT  GCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGAAGAAGAAGAAGAAGAAGAAGAAGAAG	600
С		ENNYKTTPPVLDSDGSFFLY	-
	601	ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG ++ TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC	660
c		S K L T V D K S R W Q Q G N V F S C S V	-
	661		720
С		ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT M H E A L H N H Y T Q K S L S L S P G K	-
	721	AAGGTGGAGGTGGTGGAGGTACTTACTCTTGCCACTTCGGCCCGCTGACTTGGGTTT	780
С		$\begin{array}{ccccccccccccccccccccaccaccaccaccaccacca$	-
		BamHI I	
	721	GCAAACCGCAGGTGGTTAATCTCGTGGATCC	
c	,01	CGTTTGGCGTCCCACCAATTAGAGCACCTAGG K P Q G *	
		The state of the s	

		XbaI     TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGGAGGTACTTACT	
с	1	AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCCTCCATGAATGA	
-	61	ACTTCGGCCCGCTGACTTGGGTATGTAAGCCACAAGGGGGTGGGGAAGGCGGGGGACA  TGAAGCCGGCGACTGAACCCATACATTCGGTGTTCCCCCACCCCCTCCGCCCCCCTGT F G P L T W V C K P Q G G G G G G G D K	
С		AAACTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCC	
С	121	TTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGG T H T C P P C P A P E L L G G P S V F L	
c	181	TCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCG+ AGAAGGGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGC F P P K P K D T L M I S R T P E V T C V	
С	241	TGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG  ACCACCACCTGCACTGCGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGC  V V D V S H E D P E V K F N W Y V D G V	
Č	301	TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTG	
С		ACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGCA	-
С	361	TGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGCCTGAATGGCAAGGAGTACAAGTGCA + COUNTY CO	
С	421	AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAAGGGC + + + + + + + + + + + + + + + + + + +	
c	481	AGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACC TCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGG PREPQVYTLPPSRDELTR	
	541	AGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG	600
C		V S L T C L V K G F Y P S D I A V E W E  AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG	
С	601	TCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGC S N G Q P E N N Y K T T P P V L D S D G	
С	661	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	720 -
с	721	TCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT  AGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGA  F S C S V M H E A L H N H Y T Q K S L S	
		BamHI 	
	781	CCCTGTCTCCGGGTAAATAATĠGATCC	
c		GGGACAGAGGCCCATTTATTACCTAGG L S P G K *	

	Y1	paI														
	1	   TCTAGATTTGAGTTTTAACTTTTAGAAGGAGGAATAAAATATGGGAGGTACTTACT	60													
b	1	AGATCTAAACTCAAAATTGAAAATCTTCCTCCTTATTTTATACCCTCCATGAATGA	-													
	<b>C</b> 1	CCACTTCGGCCCACTGACTTGGGTTTGCAAACCGCAGGTGGCGGCGGCGGCGGCGGTGG	120													
b	61	GGTGAAGCCGGGTGACCGAAACGTTTGGCGTCCCACCGCCGCCGCCGCCACCCH F G P L T W V C K P Q G G G G G G G	-													
b	121	TACCTATTCCTGTCATTTTGGCCCGCTGACCTGGGTATGTAAGCCACAAGGGGGTGGGGG  ATGGATAAGGACAGTAAAACCGGGCGACTGGACCCATACATTCGGTGTTCCCCCACCCCC  T Y S C H F G P L T W V C K P Q G G G	180													
D		AGGCGGGGGGACAAAACTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGG														
b	181	TCCGCCCCCTGTTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCC G G G D K T H T C P P C P A P E L L G G	240 -													
	241	ACCGTCAGTTTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC	200													
b	241	TGGCAGTCAAAAGGAGAGGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGG PSVFLFPPKPKDTLMISRTP	-													
b	301	TGAGGTCACATGCGTGGTGGTGGACCTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTG  ACTCCAGTGTACGCACCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGAC  E V T C V V V D V S H E D P E V K F N W	360													
_		GTACGTGGACGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAA														
b	361	CATGCACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTT Y V D G V E V H N A K T K P R E E Q Y N	420 -													
	401	CAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAA	400													
b	421	GTCGTGCATGGCACCACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTT S T Y R V V S V L T V L H Q D W L N G K	-													
	481	GGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTC	540													
b	-02	CCTCATGTTCACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAG E Y K C K V S N K A L P A P I E K T I S	-													
	541	CAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGA														
b		GTTTCGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGCCCTACT K A K G Q P R E P Q V Y T L P P S R D E	-													
	601	GCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACAT	660													
b		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-													
	661	CGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGT	720													
b		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-													
	501	GCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTG	700													
b	721	CGACCTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTCGACCTGTTCTCGTCCAC L D S D G S F F L Y S K L T V D K S R W	-													
	704	GCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACAC	040													
b	\8T	CGTCGTCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTG QQGNVFSCSVMHEALHNHYT														
~		BamHI														
		GCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAATGGATCC														
	841	CGTCTTCTCGGAGAGGGACAGAGGCCCATTTATTACCTAGG														
b		Q K S L S L S P G K *														

#### A-527

С

#### FIGURE 16

110		<u>u AV</u>	
		<pre>{bai</pre>	_
c	1	AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCTGTTTTGAGTGTACAG M D K T H T C P	
	61	CACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCCTCTTCCCCCCAAAAC+++++ 1 GTGGAACGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGGAGAAGGGGGGTTTTG	20
С		P C P A P E L L G G P S V F L F P P K P -	
	121	GGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCTGCACT	80
С		K D T L M I S R T P E V T C V V V D V S - GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG	
С	181	CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC H E D P E V K F N W Y V D G V E V H N A	
	241	CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA 3 GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACCACCAGTCGCAGGAGT	00
С	301	K T K P R E E Q Y N S T Y R V V S V L T -  CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG	60
с		GGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGTTTC V L H Q D W L N G K E Y K C K V S N K A -	
c	361	CCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC  GGGAGGGTCGGGGTAGCTCTTTTGGTAGAGGTTTCCGTTCCGTCGGGGCTCTTGGTG  L P A P I E K T I S K A K G Q P R E P Q	20
С	421	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	481	GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC	40
С		L V K G F Y P S D I A V E W E S N G Q P - CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT	
С	541	GCCTCTTGTTGATGTTCTGGTGCGGAGGAGGCACGACCTGAGGCTGCCGAGGAAGAAGAAGAAGA E N N Y K T T P P V L D S D G S F F L Y -	
С	601	ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG  TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGCCCTTGCAGAAGAGTACGAGGC S K L T V D K S R W Q Q G N V F S C S V	
c	661	TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGGTA  + - + + + + + + + + + + + + + + + + +	20
С	721	AAGGTGGAGGTGGCGGAGGTACTTACTCTTGCCACTTCGGCCCACTGACTTGGGTTT  TTCCACCTCCACCACCGCCTCCATGAATGAGAACGGTGAAGCCGGGTGACTGAACCCAAA G G G G G G T Y S C H F G P L T W V C	
	781	GCAAACCGCAGGGTGGCGGCGGCGGCGGCGGTGGTACCTATTCCTGTCATTTTGGCCCGC CGTTTTGGCGTCCCACCGCCGCCGCCGCCACCATGGATAAGGACAGTAAAACCGGGCG	
С		KPQGGGGGGGTYSCHFGPL- BamHI	
		TGACCTGGGTATGTAAGCCACAAGGGGGTTAATCTCGAGGATCC	

TGACCTGGGTATGTAAGCCACAAGGGGGTTAATCTCGAGGATCC

841

ACTGGACCCATACATTCGGTGTTCCCCCAATTAGAGCTCCTAGG

T W V C K P Q G G \*

#### **FIGURE 17A**

[ <u>Aat</u> II	sti	cky	en	d)	
(positi	.on	#435	8	in	pAMG21)

- 5' GCGTAACGTATGCATGGTCTCC-
- 3' TGCACGCATTGCATACGTACCAGAGG-
- $\hbox{-} CCATGCGAGAGTAGGGAACTGCCAGGCATCAAATAAAACGAAAGGCTCAGTCGAAAGACT--GGTACGCTCTCATCCCTTGACGGTCCGTAGTTTATTTTGCTTTCCGAGTCAGCTTTCTGA--$
- GGGCCTTTCGTTTTATCTGTTGTTTGTCGGTGAACGCTCTCCTGAGTAGGACAAATCCGC
   CCCGGAAAGCAAAATAGACAACAAACAGCCACTTGCGAGAGGACTCATCCTGTTTAGGCG
- CGGGAGCGGATTTGAACGTTGCGAAGCAACGGCCCGGAGGGTGGCGGGCAGGACGCCCGC GCCCTCGCCTAAACTTGCAACGCTTCGTTGCCGGGCCTCCCACCGCCCGTCCTGCGGGCG-
- CATAAACTGCCAGGCATCAAATTAAGCAGAAGGCCATCCTGACGGATGGCCTTTTTGCGT GTATTTGACGGTCCGTAGTTTAATTCGTCTTCCGGTAGGACTGCCTACCGGAAAAACGCA -

#### AatII

- TTCTACAAACTCTTTTGTTTATTTTTCTAAATACATTCAAATATGGACGTCGTACTTAAC AAGATGTTTGAGAAAACAAATAAAAAGATTTATGTAAGTTTATACCTGCAGCATGAATTG -
- TTTTAAAGTATGGGCAATCAATTGCTCCTGTTAAAATTGCTTTAGAAATACTTTGGCAGC AAAATTTCATACCCGTTAGTTAACGAGGACAATTTTAACGAAATCTTTATGAAACCGTCG -
- GGTTTGTTGTATTGAGTTTCATTTGCGCATTGGTTAAATGGAAAGTGACCGTGCGCTTAC-CCAAACAACATAACTCAAAGTAAACGCGTAACCAATTTACCTTTCACTGGCACGCGAATG-
- $\hbox{-} TACAGCCTAATATTTTTGAAATATCCCAAGAGCTTTTTCCTTCGCATGCCCACGCTAAAC-ATGTCGGATTATAAAAACTTTATAGGGTTCTCGAAAAAGGAAGCGTACGGGTGCGATTTG-$
- GATAATTATCAACTAGAGAAGGAACAATTAATGGTATGTTCATACACGCATGTAAAAATA-CTATTAATAGTTGATCTCTTCCTTGTTAATTACCATACAAGTATGTGCGTACATTTTTAT-
- TAGCAGTATGAATAGGGAAACTAAACCCAGTGATAAGACCTGATGATTTCGCTTCTTTAA ATCGTCATACTTATCCCTTTGATTTGGGTCACTATTCTGGACTACTAAAGCGAAGAAATT -
- TTACATTTGGAGATTTTTTATTTACAGCATTGTTTTCAAATATATTCCAATTAATCGGTG AATGTAAACCTCTAAAAAATAAATGTCGTAACAAAAGTTTATATAAGGTTAATTAGCCAC -
- AATATTGCCTCCATTTTTTAGGGTAATTATCCAGAATTGAAATATCAGATTTAACCATAG-TTATAACGGAGGTAAAAAATCCCATTAATAGGTCTTAACTTTATAGTCTAAATTGGTATC-
- AATGAGGATAAATGATCGCGAGTAAATAATATCACAATGTACCATTTTAGTCATATCAG-- TTACTCCTATTTACTAGCGCTCATTTATTATAAGTGTTACATGGTAAAATCAGTATAGTC -

- $\hbox{-} \texttt{GCAAGTTTTGCGTGTTATATATCATTAAAACGGTAATAGATTGACATTTGATTCTAATAA-}$
- -CGTTCAAAACGCACAATATATAGTAATTTTGCCATTATCTAACTGTAAACTAAGATTATT-

#### FIGURE 17B

- ATTGGATTTTTGTCACACTATTATATCGCTTGAAATACAATTGTTTAACATAAGTACCTG - TAACCTAAAAACAGTGTGATAATATAGCGAACTTTATGTTAACAAATTGTATTCATGGAC -
- TAGGATCGTACAGGTTTACGCAAGAAAATGGTTTGTTATAGTCGATTAATCGATTTGATT - $\hbox{-}ATCCTAGCATGTCCAAATGCGTTCTTTTACCAAACAATATCAGCTAATTAGCTAAACTAA-\\$
- CTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGTTAACGCGTTGGAATTCGA  $\hbox{-} {\tt GATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCAATTGCGCAACCTTAAGCT-}$

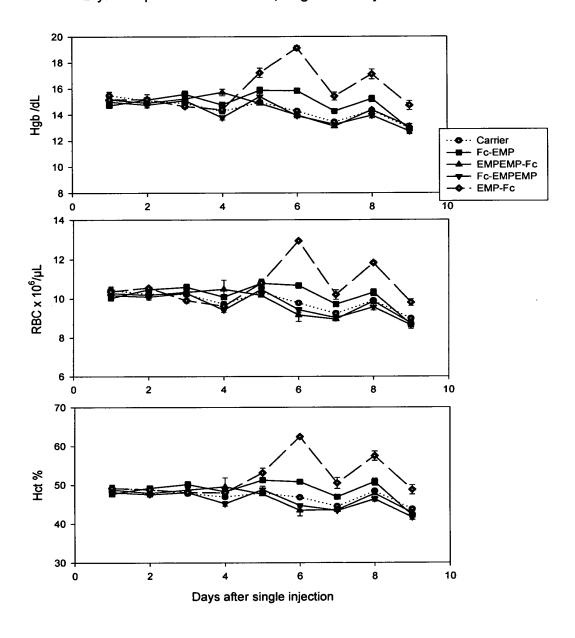
#### <u>Sac</u>II

- -GCTCACTAGTGTCGACCTGCAGGGTACCATGGAAGCTTACTCGAGGATCCGCGGAAAGAA- $\hbox{-} \textbf{CGAGTGATCACAGCTGGACGTCCCATGGTACCTTCGAATGAGCTCCTAGGCGCCTTTCTT-} \\$
- GAAGAAGAAGAAGCCCGAAAGGAAGCTGAGTTGGCTGCCACCGCTGAGCAATA - $\hbox{-}CTTCTTCTTCTTCGGGCTTTCCTTCGACTCAACCGACGGTGGCGACTCGTTAT-\\$
- $\hbox{-} ACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTTGCTGAAAGGAGG \hbox{-} {\tt TGATCGTATTGGGGAACCCCGGAGATTTGCCCAGAACTCCCCAAAAAACGACTTTCCTCC-}$
- -AACCGCTCTTCACGCTCTTCACGC 3'

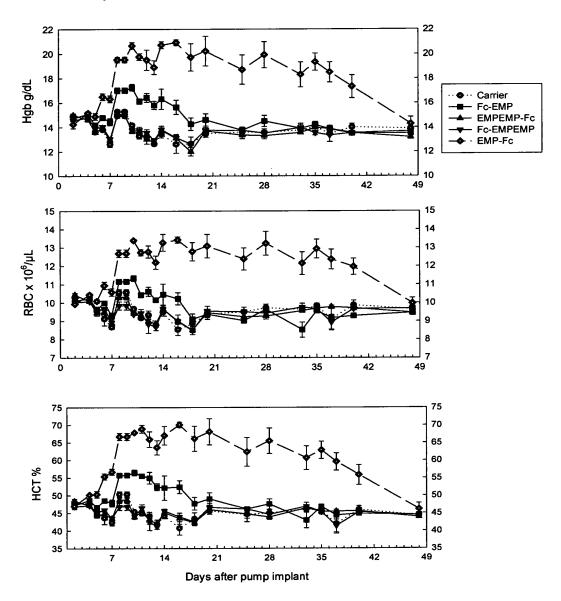
[SacII sticky end]

-TTGGCGAGAAGTGCGAGAAGTG 5' (position #5904 in pAMG21)

Erythroid parameters EMP-Fc, single bolus injection.



Normal female BDF1 mice treated with 100ug/kg EMP-Fc in 7-day micro osmotic pumps



## FIGURE 19A

	NdeI	1																											
	1	CATA	TGGA				CAC												GGG	ACCG	60								
	1	GTAT	ACCT	•			•				•								CCC	rggc									
a		M	D	K	Т	Н	Т	С	P	P	С	P	A	P	E	L	L	G	G	P	-								
	61	TCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG+															120												
	<b>.</b>	AGTC	AGAA	AGGA	GAA	.GGG	GGG	ттт	TGG	GTT	CCT	GTG	GGA	GTA	CTA	GAG	GGC	CTG	GGG	ACTC									
a		s v	F	L	F	P	P	K	P	K	D	Т	L	M	I	s	R	Т	P	E	-								
	121	GTCA CAGT		-+-			+				+			-+-			+			+	180								
a		v 1	C	v	v	v	D	v	s	н	E	D	P	E	v	ĸ	F	N	W	Y	-								
	1.01	GTGG	ACGG																CAA	CAGC	240								
	181			•							•								GTT	GTCG	+ 240 G								
a		v r	G	v	E	V	Н	N	A	K	Т	K	P	R	E	E	Q	Y	N	S	-								
	241	ACGT	ACC				CGT												CAA	GGAG	300								
	241	TGCA	TGGC	•							•								GTT	CCTC									
a		T Y	R	V	V	s	v	L	T	V	L	Н	Q	D	W	L	N	G	K	E	-								
	301	TACA	AGTO	GCAA	GGT	CTC	CAA	CAA	AGC	CCT	CCC	AGC	CCC	CAT	CGA	GAA	AAC +	CAT	CTC	CAAA +	360								
		ATGT	TCAC	CGTT	'CCA	GAG	GTT	GTT	TCG	GGA	.GGG	TCG	GGG	GTA	GCT.	CTT	TTG	GTA	GAG	GTTT									
a		Y K	C	K	V	S	N	K	A	L	P	A	P	I	Ε	K	Т	I	S	K	-								
	361	GCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG														420													
		CGGI	TTCC	CCGT	CGG	GGC	TCT	TGG	TGT	CCA	CAT	GTG	IGGA	.CGG	GGG	TAG	AGGGCCCTACTCGAC												
a		A K	G	Q	P	R	E	P	Q	V	Y	Т	L	P	P	S	R	D	E	L	-								
	421		AGAA	- + -			+				+			-+-			+			+	480								
																	GTC	GCT	GTA	GCGG									
a			N															D	I		-								
	481			+ -			+	- <b></b>			+			-+-			+			GCTG + CGAC	540								
a		V F	. w	E	s	N	G	Q	P	E	N	N	Y	ĸ	т	т	P	P	v	L	-								
		GACT	CCG <i>I</i>	ACGG	CTC	стт	стт	CCT	СТА	CAG	CAA	GCI	CAC	:CGI	'GGA	CAA	GAG	CAG	GTG	GCAG									
	541			+ -			+				+			-+-			+			CGTC	600								
a		D S	D	G	s	F	F	L	Y	s	K	L	T	v	D	K	S	R	W	Q	-								

# FIGURE 19B

	601				-+-			+				+			-+-			+			GCAG + CGTC	660
a		Q	G	N	v	F	s	С	s	v	M	Н	E	A	L	Н	N	Н	Y	Т	Q	-
	661				-+-			+				+			-+-			+			CTAC + GATG	720
a		ĸ	s	L	s	L	s	P	G	ĸ	G	G	G	G	G	D	F	L	P	Н	Y	-
											Ва	mHI I										
	AAAAACACCTCTCTGGGTCACCGTCCGTAATGGATCC 721																					
		17	NT	m		т.	~	ы	D	ъ	*											

## FIGURE 20A

		Nd	eI																		
	1		ATGG				GCA												rgg <i>i</i>		60
	1		TACC																ACC		00
a		]	M D	F	L	P	Н	Y	K	N	T	s	L	G	Н	R	P	G	G	G	-
	61		GGGGZ CCCC	+ -			+				+			-+-			+			+	120
a			G D	K	т	н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
a		•	GTTT!		_		_	_	-	_	-	_		_		_ СтС(	CCG	GAC	ceer	TGAG	
	121			+ -			+				+			- + -			+			+	180
			CAAA	_																	
a		_	V F	L	F	Р	P	K	P	K	D	Т	L	М	Ι	S	R	T	Р	Е	-
	181		ACAT	+ -			+				+			-+-			+			+	240
		CAG	TGTA	CGCA	CCA	.CCA	.CCT	GCA	CTC	GGT	GCT	тст	GGG	ACT	CCA	GTT	CAA	GTT	GAC	CATG	
a		V	т с	V	V	V	D	V	s	Н	E	D	P	E	V	K	F	N	W	Y	-
	241		GACG(	+ -			+				+			-+-			+			+	300
a		v	D G	v	E	v	Н	N	A	ĸ	т	ĸ	P	R	E	E	Q	Y	N	s	-
	301		TACC	+ -			+				+			-+-			+			+	360
a			Y R	v	v	s	v	L	Т	v	L	н	0	D	W	L	N	G	К	 Е	_
a		_	AAGT	•	•	-	·	_	-	-			_					_			
	361		TTCA	+-		<b>-</b>	+				+			-+-			+			+	420
a		Y	к с	K	v	s	N	ĸ	Α	L	P	A	P	I	E	K	${f T}$	I	s	K	-
	421		AAAG( TTTC(	+ -			+				+			-+-			+			+	480
a		Α	K G	Q	P	R	E	P	Q	v	Y	т	L	P	P	s	R	D	E	L	-
	481		AAGA TTCT	+-			+				+			-+-			+			+	540
a			K N																		-
	541		GAGT(  CTCA(	+ -			+				+			-+-			+			+	600
a		v	E W	E	s	N	G	Q	P	E	N	N	Y	ĸ	т	${f T}$	P	P	v	L	-

#### FIGURE 20B

	601				-+-			+				+			- + -			+			GCAG + CGTC	660
a		D	s	D	G	s	F	F	L	Y	S	ĸ	L	T	v	D	K	s	R	W	Q	-
	661	GTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTC															720					
a		Q	G	N	v	F	S	С	s	v	M	Н	Ε	A	L	Н	N	Н	Y	т	Q	-
	721				-+-			+	<b>-</b>		ATA.	mHI   ATG( +			- + -	76	1					
a		K	s	L	S	L	s	P	G	K	*											

#### FIGURE 21A

	No	leI 																				
	1				-+-			+				+			- + -			+ -				60
_				D	31"1". K	TTG.	AGT H	GTG T	C C	AGG P	rgg. P	AAC.	AGG P	A	AGG P	E	L L	JGA L	G	G	rGGC	_
a				_		_		_	_	_	_	_	Ē.					_	_	_	rgag	
	61				+-			+				+			-+-			+			ACTC	120
a		s	v	F	L	F	P	P	K	P	K	D	т	L	М	I	S	R	т	P	E	-
_		GTC	ACA	TGC	CGT	GGT	GGT	GGA	CGT	GAG	CCA	CGA.	AGA	CCC	TGA	GGT	CAA	GTT(	CAAC	CTGC	TAC	
	121				-+-			+				+			-+-			+	- <b>-</b> -		CATG	180
a		v	т	c	v	v	v	D	v		н	E	D	P	E	v		F	N	W	Y	_
u		•	_	•	•	•	•	_	-					_		-		- GCA	GTA(	CAAC	CAGC	
	181				+-			+				+			-+-			+			TCG	240
_					V		v				K	Т	K	P		E	E	0	Y	N	s	_
a		•	_	_					_					_		_	_	~	_		GGAG	
	241				- + -			+				+			-+-			+			+	300
														_					_	K	E	_
a		T	Y 	R	V	-	S 	V 	L	T	V	L	Н	Q aaa	D Com	W	L	N	G Tame		_	-
	301				-+-			+				+			-+-			+			CAAA +	360
																					STTT	
a		Y	K	С	K	V	S	N	K	Α	L	P	A	P	I	E	K	T	I	S	К	-
	361				- + -			+				+			-+-			+			GCTG	420
		CGG	TTT	CCC	CGT	CGG	GGC	тст	TGG	TGT	CCA	CAT	GTG	GGA	CGG	GGG'	TAG	GGC	CCT	ACTO	CGAC	
a		Α	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	s	R	D	Е	L	-
	421	ACC																			CGCC	480
		TGG	TTC	TTC	GGT(	CCA	GTC	GGA	CTG	GAC	GGA	CCA	GTT	TCC	GAA	GAT.	AGG	GTC	GCT	GTA(	GCGG	
a		Т	K	N	Q	V	S	L	T	С	L	V	K	G	F	Y	P	S	D	I	Α	-
	481	GTO	GAG	TG	3GA	GAG	CAA	TGG	GCA	GCC	GGA	GAA +	CAA	CTA	CAA	GAC	CAC	GCC' +	TCC	CGT	GCTG	540
	-0-	CAC	CTC	CAC	CCT	CTC	GTT	ACC	CGT	CGG	ССТ	CTT	GTT	GAT	GTT	CTG	GTG	CGG	AGG	GCA	CGAC	
a		v	E	W	E	S	N	G	Q	P	E	N	N	Y	K	T	Т	P	P	V	L	-
	5/1	GAC	TCC	GAG	CGG(	CTC	CTT	CTT	CCT	CTA	CAG	CAA +	GCT	CAC	CGT	GGA	CAA	GAG	CAG	GTG	GCAG	600
	741																				CGTC	
a		D	S	D	G	s	F	F	L	Y	S	K	L	Т	V	D	K	S	R	W	Q	-

## FIGURE 21B

	601	CA	GGG	GAA	CGT	CTT	CTC.	ATG	CTC	CGT	GAT	GCA	TGA	GGC	TCT <sup>-</sup> -+-	GCA	CAA	CCA	CTA	CAC	GCAG	660
	901	GT	CCC	CTT	GCA	GAA		•				•									CGTC	
a		Q	G	N	v	F	S	С	S	V	M	Н	Ε	A	L	Н	N	Н	Y	T	Q	-
	661				-+-			+				+			-+-			+			GGGT + CCCA	720
a		K	s	L	s	L	s	P	G	K	G	G	G	G	G	F	E	W	Т	P	G	-
											Ва	mHI.										
	721				-+-		.CGC  'GCG	+				+			-+-		763					
2		v	TAT	0	Ð	v	Δ	т.	P	Τ.	*											

## FIGURE 22A

		Nde I	eΙ																		
	1		ATGTT																		60
	-		ГАСАА																		
a		1	M F	E	W	T	P	G	Y	W	Q	P	Y	A	L	P	L	G	G	G	-
	61		GGGA	CAA	AAC	TCA										ACT		GGG(	GGG/	ACCG	120
	01		CCCT	GTT	TTG	AGT												CCC	CCC'	rggc	
a		G (	G D	K	т	Н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
	121	TCA	GTTTT	CCT	СТТ											CTC					180
	121	AGT	CAAAA	GGA	GAA																100
a		s '	V F	L	F	P	P	K	P	K	D	T	L	M	I	s	R	Т	P	E	-
	101		ACATG																		240
	181		TGTAC																		240
a		v '	т с	v	v	V	D	V	s	Н	E	D	P	E	v	ĸ	F	N	W	Y	-
	0.44	GTG	GACGG	CGT	GGA	.GGT	GCA	TAA	TGC	CAA	GAC	AAA	.GCC	GCG	GGA	GGA	GCA	GTA	CAA	CAGC	200
	241		CTGCC																		300
a		v :	D G	v	E	v	Н	N	A	K	т	ĸ	P	R	E	E	Q	Y	N	s	-
		ACG'	TACCG															TGG	CAA	GGAG	260
	301	TGC	ATGGC													CGA		ACC	GTT	CCTC	360
a		T ·	Y R	v	v	s	v	L	Т	v	L	Н	Q	D	W	L	N	G	к	E	-
		TAC	AAGTG																		420
	361	ATG	TTCAC													CTT					420
a		Y :	к с	ĸ	v	s	N	K	A	L	P	A	P	I	E	ĸ	т	I	s	K	-
		GCC.	AAAGG	GCA																	480
	421	CGG	TTTCC	CGT																CGAC	400
a		A :	K G	Q	P	R	E	P	Q	V	Y	т	L	P	P	s	R	D	E	L	-
		ACC.	AAGAA	CCA	GGT	CAG	CCT	GAC	CTG	CCT	GGT	CAA	AGG	СТТ	CTA	TCC	CAG	CGA	CAT	CGCC	E 4 O
	481		TTCTI																		340
a		T	K N	Q	v	s	L	${f T}$	С	L	v	ĸ	G	F	Y	P	s	D	I	Α	-
		GTG	GAGTG	GGA	GAG	CAA	TGG	GCA	.GCC	GGA	GAA	.CAA	CTA	CAA	.GAC	CAC	GCC	TCC	CGT	GCTG	<b>600</b>
	541		CTCAC																		600
a		v	E W	E	s	N	G	Q	P	E	N	N	Y	K	т	т	P	P	v	L	-

#### FIGURE 22B

	601				-+-			+				+			-+-			+			GCAG + CGTC	660
a		D	s	D	G	s	F	F	L	Y	s	K	L	т	v	D	K	s	R	W	Q	-
	661				-+-			+				+			-+-			+			GCAG + CGTC	720
a		Q	G	N	V	F	S	С	s	V	M	Н	E	A	L	Н	N	Н	Y	Т	Q	-
											Ва	mHI 										
	721				-+-			+				ATĠ + TAC			757							
а		к	S	T.	s	L	S	Р	G	K	*											

## FIGURE 23A

	Nd	leI																				
	1				-+-			+			·	+			-+-			-+-			.CCG	60
		GTA	AT.	CTC	GTT'	rtgi	AGT	GTG!	rac:	AGG:	rgg	CAC	GGG'	rcg:	rggz	ACT:	rgac	GAC	ccc	CCT	GGC	
a			M	D	K	Т	H	Т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
	61		GTT	rtt(	CCT	CTT	CCC	ccc	AAA	ACC	CAA	GGA(	CAC	CCT	CAT(	GAT(	CTCC	CCGC	ACC	CCI	'GAG	120
	91	AGT	CAZ	AAA	GGA	GAA	GGG														CTC	
a		s	V	F	L	F	P	P	ĸ	P	K	D	T	L	M	I	s	R	Т	P	E	-
		GTC	CAC	ATG	CGT	GGT	GGT	GGA	CGT	GAG	CCA	CGA	AGA	CCC'	TGA(	GGT	CAAC	STTC	CAAC	TGG	TAC	190
	121	CAC	TG	 TAC	-+- GCA	CCA	CCA	CCT	GCA	CTC	GGT	GCT	TCT	GGG:	ACT	CCA	GTT	CAAC	3TTC	SACC	CATG	100
a		v	т	С	v	v	v	D	v	s	Н	E	D	P	E	v	ĸ	F	N	W	Y	-
		GTO	GAG	CGG	CGT	GGA	GGT	GCA	TAA	TGC	CAA	GAC.	AAA	GCC	GCG	GGA	GGA	GCA	GTA(	CAAC	CAGC	0.4.0
	181	CAC	CTC	 GCC	- + - GCA	CCT	CCA	+ CGT	 ATT	acg	 GTT	+ CTG	 TTT	CGG	-+- CGC	CCT	CCT	CGT	CAT	GTTC	TCG	240
a		v	D	G	V	E	v	н	N	A	K	$\mathbf{T}$	ĸ	P	R	E	E	Q	Y	N	s	-
		ACC	TA	CCG	TGT	GGT	CAG	CGT	сст	CAC	CGT	ССТ	GCA	CCA	GGA	CTG	GCT	GAA'	rgg	CAAC	GAG	
	241				-+-			+				+			-+-			+	- <b></b> ·		CCTC	300
a		т	Y	R		v		v	_	т		L		0	D	W	L	N	G	ĸ	Е	-
u.		_	=					CAA	CAA	AGC	ССТ	ccc	AGC	CCC	САТ	CGA	GAA	AAC	CAT	CTC	CAAA	
	301				-+-			+				+			-+-			+			+ 3TTT	360
2		Y	K	C	K	v		N	K	A	L	P	A	P	I	E	ĸ	т	I	s	K	_
a		_		_		•	_					_		_	- GCC	CCC	ATC	CCG	GGA'	rgao	SCTG	
	361				-+-			+				+			-+-			+			+ CGAC	420
							R	E E		0								R	D	E	L	_
a					Q			_	_	~									_	_ ሮልጥረ	CGCC	
	421				-+-			+				+			-+-			+			+ GCGG	480
																						_
a																					A CCTC	
	481				-+-		. <b></b>	+				+			-+-			+			GCTG	540
																					CGAC	
a																					L	
	541				-+-							+			-+-			+			GCAG	600
		CT	GAG	GC1	rgcc	CGAC	GA.	AGAA	AGGA	GAT	GTC	GTT	CGA	GTG	GCA	CCI	GTT	CTC	GTC	CAC	CGTC	
a		D	S	D	G	S	F	F	L	Y	S	K	L	${f T}$	V	D	K	S	R	W	Q	-

## FIGURE 23B

	601		<b></b> -		-+-			+				+			-+-			+			GCAG + CGTC	660
a		Q	G	N	v	F	s	С	s	v	M	Н	E	A	L	Н	N	Н	Y	т	Q	-
	661				-+-			+				+			-+-			+			TGAC + ACTG	720
a		ĸ	S	L	s	L	s	P	G	K	G	G	G	G	G	v	E	P	N	С	D	-
																В	amH	I 				
	721				-+-			+				TGA + ACT			-+-			+		77	3	
_		_	ш	7.7	M	TAT	127	TA7	-	C	F	┎	Ð	τ.	*							

#### FIGURE 24A

	INC	ıeı I																				
	1				-+-			+				+			-+-			+			ACGT	60
		GT	ATA	CCA	ACT	TGG	CTT	GAC	ACT	GTA	GGT.	ACA.	ATA(	CAC	CCT'	TAC	CCT"	rac.	AAAA	ACT".	rgca	
a			M	V	E	P	N	С	D	I	Н	V	M	W	E	W	E	С	F	Е	R	-
	61	CTC																			ACTC	120
		GA																			rgag	
a		L	G	G	G	G	G	D	ĸ	т	Н	T	С	P	P	С	P	A	P	E	L	-
	404		GGG																		CTCC	100
	121		CCC						GGA												GAGG	180
a		L	G	G	P	s	v	F	L	F	P	P	ĸ	P	K	D	т	L	M	I	S	-
		CG																			CAAG	240
	181	GC			•				GCA												STTC	240
a		R	т	P	E	v	т	С	v	v	v	D	v	s	Н	E	D	P	E	v	ĸ	-
																					GGAG	
	241																				CCTC	300
a		F	N	W	Y	v	D	G	v	E	v	Н	N	A	K	т	K	P	R	E	E	-
	301				-+-			+				+			-+-			+				360
		GT	CAT	GTT	GTC	GTG	CAT	GGC	ACA	CCA	GTC	GCA	GGA	GTG	GCA	GGA	CGT	GGT	CCT	GAC	CGAC	
a		Q	Y	N	S	Т	Y	R	v	V	S	V	L	T	V	L	Н	Q	D	W	L	-
•	361	AA'							CAA												GAAA	420
	301	TT																			CTTT	
a		N	G	K	E	Y	K	С	K	v	s	N	K	A	L	P	A	P	I	E	K	-
	421																				ATCC	480
	421																				ragg	100
a		T	I	s	K	A	K	G	Q	P	R	E	P	Q	v	Y	T	L	P	P	S	-
	401	CG	GGA	TGA	GCT	GAC	CAA	GAA	CCA	GGT	CAG	CCT	GAC	СТG	ССТ	GGT	CAA	AGG	CTT	CTA	rccc	540
	401																				AGGG	3.10
a		R	D	E	L	Т	ĸ	N	Q	v	s	L	т	С	L	v	K	G	F	Y	P	-
		AG	CGA	CAT	CGC	CGT	'GGA	.GTG	GGA	GAG	CAA	TGG	GCA	GCC	GGA	GAA	CAA	CTA	CAA	GAC	CACG	600
	541	TC	GCT	GTA	- + - GCG	GCA	CCT	CAC	ССТ	CTC	GTT	ACC	CGT	CGG	CCT	CTT	GTT	GAT	GTT	CTG	GTGC	800
a		s	D	I	Α	v	E	W	E	s	N	G	Q	P	E	N	N	Y	ĸ	т	т	-

## FIGURE 24B

	601				-+-			+				+			-+-			+			CAAG + GTTC	660
a		P	P	v	L	D	s	D	G	s	F	F	L	Y	S	K	L	T	v	D	K	-
	661				-+-			+				+			-+-			+			CAAC + GTTG	720
a		s	R	W	Q	Q	G	N	V	F	s	С	S	V	M	Н	E	A	L	Н	N	-
	721				-+-			+				+			-+-	ACT		 .GGA +		77	3	
		GT	GAT	GTG	CGT	CTT	CTC	GGA	GAG	GGA	CAG	AGG	CCC	TTA:	PAT	TGA	GCI	CCI	'AGG	}		
_		н	v	т	0	ĸ	S	т.	S	T,	S	P	G	K	*							

#### FIGURE 25A

	Nd	leĮ																				
	1				- +			+				+		<del>.</del> .	· <b>+ -</b> -			-+-				60
	-	GTA	TAC	CTO	GTTT	rtg	AGT(	GTG'	TAC	AGG"	rggz	AAC	AGG:	rcga	AGGC	CTT	'GAC	GAC	CCC	CCI	'GGC	
a			M	D	K	T	Н	Т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
	<i>c</i> 1		GTC	TTC	CCTO	CTT	CCC	CCC	AAA	ACC	CAA	GGA(	CAC	CCT	CATO	TAE	CTCC	CGG	ACC	CCT	GAG	120
	61	AGT	CAC	AA	GGA	GAA	GGG														CTC	
a		s	v	F	L	F	P	P	K	P	K	D	т	L	M	I	s	R	T	P	E	-
		GTC	ACA	TG	CGT	GGT	GGT	GGA	CGT	GAG	CCA	CGA	AGA	ccc	rgac	GTO	CAAC	STTC	CAAC	CTGG	TAC	100
	121	CAG	TGT	AC	-+- GCA	CCA	CCA	+ CCT	GCA	 CTC	GGT	+ GCT'	 rcte	GGG	- + - АСТ(	CCA	GTT(	CAAC	TTC	GACC	CATG	180
a		v							v							v		F	N	W	Y	-
u														GCC	GCGC	GAG	GGA	GCAC	3TAC	CAAC	CAGC	
	181		<b>-</b> -		-+-			+				+			- + -			+ -	:		+	240
		CAC																_	Y	N	STCG	_
a		V	_	_	V		V		N		K	Т	K	P	R	Е	Е	Q	_		_	
	241	ACC	TAC	CCG	TGT:	GGT	CAG	CGT	CCT	CAC	CGT	CCT	GCA	CCA	GGA( - + -	CTG	GCT( 	GAA'. +	rgg(	CAAC	GGAG	300
		TGC	CATO	GC.	ACA	CCA	GTC	GCA	.GGA	GTG	GCA	GGA	CGT	GGT	CCT	GAC	CGA	CTT	ACC	GTT(	CCTC	
a		т	Y	R	v	V	s	v	L	Т	V	L	Н	Q	D	W	L	N	G	K	E	-
		TAC	CAAC	ЭТG	CAA	GGT	CTC	CAA	CAA	AGC	CCT	ccc	AGC	ccc	CAT	CGA	GAA	AAC	CAT	CTC	CAAA +	360
	301	ATO	GTT(	CAC	-+- GTT	CCA	GAG	GTT	GTT	TCG	GGA	.GGG	TCG	GGG	GTA	GCT	CTT'	TTG	GTA	GAG	GTTT	300
a		Y	ĸ	С	K	v	s	N	K	A	L	P	Α	P	I	E	K	Т	I	S	K	-
		GC	CAA	AGG	GCA	GCC	cce	AGA	ACC	ACA	GGT	GTA	CAC	CCT	GCC	ccc	ATC	CCG	GGA	TGA	GCTG	
	361				-+-			+				+			-+-			+			+ CGAC	420
a			ĸ		Q							Y					s	R	D	E	L	=
		AC	CAA	GAA	CCA	GGT	CAC	CCI	GAC	CTG	CCT	GGT	CAA	AGG	СТТ	СТА	TCC	CAG	CGA	CAT	CGCC	
	421				-+-			+				+			-+-			+			+ GCGG	480
																					A	_
a																						
	481				-+-			+				+			-+-			+			GCTG	540
		CA	CCT	CAC	CCT	CTC	CGTT	CACC	CCGT	'CGG	CCI	CTT	'GT'I	'GA'1	'GTT	CTG	GTG	CGG	AGG	GCA	CGAC	
a		v	E	W	E	S	N	G	Q	P	E	N	N	Y	K	Т	Т	P	P	V	L	-
		GA	CTC	CGA	CGG	CTC	CTT	CTI	rcci	CTA	CAC	CAA	GCI	CAC	CGT	GGA	CAA	GAG	CAG	GTG	GCAG	600
	541	CT	GAG	GCI	GCC	GAC	GA.	AGAZ	AGGA	GAT	GTC	GTI	CGA	GTG	GCA	CCI	'GTT	CTC	GTC	CAC	CGTC	
a		D	s	D	G	s	F	F	L	Y	s	ĸ	L	T	V	D	K	S	R	W	Q	-

## FIGURE 25B

	601	CA	GGG	GAA(	CGT	CTT	CTC	-													GCAG	660
	001	GT	ccc	CTTC	GCA(	GAA	GAG														CGTC	
a		Q	G	N	v	F	s	С	S	V	М	Н	E	A	L	Н	N	H	Y	Т	Q	-
	661				-+-			+				+			-+-			+			GGGT + CCCA	720
A		K	s	L	S	L	s	P	G	K	G	G	G	G	G	С	Т	Т	Н	W	G	-
	721		CAC(		-+-	CTA		GAT +				748										

## FIGURE 26A

	No	leI I																													
	1				- + -			+ -		. <b></b> .	4	- <b>-</b> -	<b>-</b> -		· <b>+ -</b> -			+ -			GGT +	60									
•		GTA	ATA(	CAC	GTG	GTG(	GGT	GAC	CCC	AAA(	STGO	GAC	CACC	3CCI	ACCI	rcco	3CC#	ACCC	ссто		'CCA										
а			M	С	Т	Т	Н	W	G	F	Т	L	С	G	G	G	G	G	D	K	G	-									
	61				-+-			+				<b></b>			- +			+ -				120									
		CCI	rcc	GCC.	ACC	CCT	GTT'	rtg/	AGT(	GTG'	rac <i>i</i>										CCC										
a		G	G	G	G	D	K	T	Н	T	С	_	P	С	P	A	P 	E	L		G	-									
	121			- <b></b>	-+-			+				+			- + -			+ -	<del>-</del> ·		SACC	180									
		CC	rgg	CAG	TCA	AAA															CTGG										
a		G	P	_		F					K							I 	S	R	T	-									
	181				-+-			+				+			-+-			+			CAAC + 240										
		GG	АСТ	CCA	GTG	TAC	GCA	CCA	CCA	CCT	GCA(	CTC								_	GTTG										
a		P	_	V	_	•	V		-		V	_	H	E	D	P	E	V	K	F	N	-									
	241		TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTAC+++++++-														300														
		AC	CAT	'GCA	.CCT	GCC	GCA	CCT	CCA	CGT	ATT.	ACG																			
a		W	_	V	_	G	V	Е	V	Н	N	A	K	T	K	P	R	E	E	Q	Y	-									
	301		AACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGC+++ 360 TTGTCGTGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCG																												
		TT	GTC	GTG	CAT	'GGC	ACA	CCA																							
a		N	S	Т	Y	R	V	V	_	V			٧			Q	D	W	_	N		-									
	361		AAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATC															420													
		тт																				_									
a 4		K	_	_	_		K						L			Р	I	E	K	T	I	-									
	421		TCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGAT  AGGTTTCGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTA														480														
																						_									
a							Q													R											
	481	- <b>-</b>			-+-		<b></b>	+				+			-+-			+			CGAC	540									
																					GCTG	_									
a							Q														D mccc	-									
	541				+ -			+				+			-+-			+			TCCC	600									
																					AGGG	_									
a		I	Α	V	E	W	E	S	N	G	Q	Ρ	E	N	N	Y	K	$\mathbf{T}$	т	Р	P	-									



## FIGURE 26B

	601				-+-			+				+			-+-			+			CAGG + GTCC	660
a		v	L	D	s	D	G	S	F	F	L	Y	S	K	L	T	V	D	K	s	R	-
	661				-+-			+	,-			+			- + -			+			CTAC + GATG	720
a		W	Q	Q	G	N	v	F	S	С	S	V	M	Н	E	A	L	Н	N	Н	Y	-
		BamHI																				
	721	ACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAATGGATCC L																				
a		т	Ω	ĸ	g	т.	g	Τ.	S	Þ	G	ĸ	*									